



Today more than ever before life must be characterized by a sense of Universal responsibility, not only nation to nation and human to human, but also human to other forms of life.

Dalai Lama, quoted in  
*A Cry from the Forest*, 1987

## Forum

### Shedding Light on Skin Cancer

A rare disease in which people develop skin cancers at the mildest exposure to sunlight may shed new light on how other environmental factors produce disease in humans.

Both ultraviolet radiation from the sun and pollutants produced from cigarettes and fossil fuels cause damage in human cells that may be repaired by the same set of crucial cellular enzymes, say researchers at the University of Texas Medical Branch in Galveston. At the university's Sealy Center for Molecular Science, scientists are focusing on a group of genes that is responsible for repairing damage that occurs in DNA. In its first year, the Sealy Center has brought together the largest group of DNA repair experts in the United States: 7 scientists, each with a research staff of up to 25 people.

An example of the kind of research fostered by the center is the recent finding published in *Nature* October 28. A team led by molecular biologist Satya Prakash uncovered the cause of one form of the genetic disorder xeroderma pigmentosum. Patients with the disease cannot tolerate ultraviolet radiation. Their skin burns severely at the slightest exposure to the sun, they have rashes, and they suffer from a variety of skin cancers, including melanoma and basal cell carcinoma. They generally die by age 20.

Researchers knew that people with xeroderma pigmentosum had a defective gene, called *XPD*, but they didn't know the role of the gene's protein. Now Prakash and his research team, who came to the Sealy Center from the University of Rochester, have purified the protein and discovered that it is a DNA helicase, whose role is to unwind the DNA double-helix.

Now the pathogenesis of the disease has become clear: ultraviolet radiation routinely causes base pairs in double-stranded DNA to fuse, producing a distorting bulge. This damage is normally detected by the *XPD* enzyme as it uncoils the DNA in preparation for other repair enzymes to snip out and repair the damage. "But when the enzyme is disabled, the damage remains, and cancer likely results due to mutations in genes that normally protect the cell against uncontrolled growth," said Prakash.

So far, seven genes have been identified that act in concert to repair DNA damage. Disease can result when mutations occur in any of these genes or when environmental insult damages the action of the enzymes. Identifying the disorders and their triggers are the goals of the Galveston researchers.

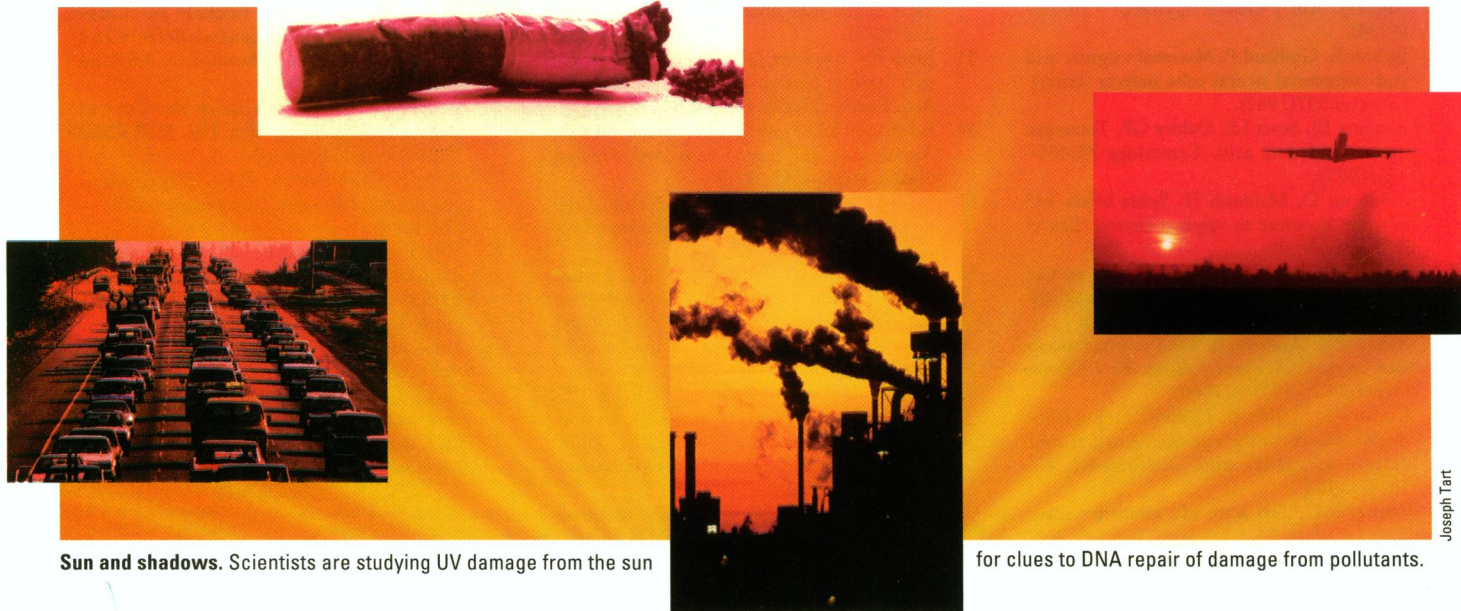
Research has shown that the same kind of pathway that helps to repair UV damage is potentially involved in removing

chemicals that attach to DNA such as products of fossil fuel combustion, said center researcher Stephen Lloyd. In these cases, the chemicals, known as polycyclic aromatic hydrocarbon compounds, don't fuse DNA bases but attach directly onto base pairs, causing distortions in the DNA.

Lloyd, who came to Galveston from Vanderbilt University, plans to collaborate with Prakash to determine how the cellular repair system responds to each different compound. He will work with Thomas Harris, an expert in DNA synthesis, to attach different chemicals to synthesized DNA, after which Prakash will experimentally subject the DNA lesion to the full complement of seven repair enzymes to see if they can repair the damage. Researchers can then learn if cellular repair systems can clear specific environmental damage. Said Lloyd, "It will help us make predictions about the true impact chemicals found throughout our daily lives have on our health."

### Gasoline, Asbestos, and Dioxin

New data on the health hazards of gasoline, chrysotile asbestos, and dioxin were presented at the annual conference of the Collegium Ramazzini, an international group of scientists dedicated to the study of issues of environmental and occupational health. The collegium, created in 1982



Sun and shadows. Scientists are studying UV damage from the sun

for clues to DNA repair of damage from pollutants.